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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/736,267	10/24/96	BACKSTROM K	06275/004001

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EXAMINER	
DUFFY, P	

ART UNIT	PAPER NUMBER
1645	28

DATE MAILED: 01/22/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/736,267	Blackstrom
Examiner	**Group Art Unit**
Ducey	1645

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 11-2-98 & 12-21-98.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☒ Claim(s) 1-17, 21, 22, 26-32, 50-100 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☒ Claim(s) 1-17, 21, 22, 26-32, 50-100 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s)._____

☒ Notice of Reference(s) Cited, PTO-892

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Interview Summary, PTO-413

☐ Notice of Informal Patent Application, PTO-152

☐ Other_____

Office Action Summary

Response to Amendment

1. The amendment filed 11-2-98 and information disclosure statement filed 12-21-98 have been entered into the record.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Withdrawn

3. The rejection of claims 1-13, 17- 20, 31-44, 48, and 49 are rejected under 35 U.S.C. 102(e) as being anticipated by Illum (U.S. Patent No. 5,707,644, filed May 21, 1993) is withdrawn based on applicants amendments.

4. The rejection of claims 1, 3-12, 17, 19, 20, 21, 26, 27, 28, 34-43 and 50-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Durrani et al (WO 91/16882, published 14 November 1992) is withdrawn based on lack of evidence that the phospholipids in Durrani et al are enhancers of absorption.

Rejections Maintained

Double Patenting

5. Claims 1-3, 11-16, and new claims 61-100 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 5,581,998 is maintained for reasons previously made of record. The terminal disclaimer filed with the response has not been considered because it was not accompanied by the appropriate fee and the terminal disclaimer had non-initialed, non-dated changes to the

company name. Correction of the terminal disclaimer and the fee are required in order to obviate the outstanding obvious double patenting rejections.

6. Claims 21, 22, 28-32 and 51-100 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 5,506,203 is maintained for reasons previously made of record for claims 21, 22, 28-32 and 51-60. The terminal disclaimer filed with the response has not been considered because it was not accompanied by the appropriate fee and the terminal disclaimer had non-initialed, non-dated changes to the company name. Correction of the terminal disclaimer and the fee are required in order to obviate the outstanding obvious double patenting rejections.

Claim Rejections - 35 USC § 112

7. Claims 1-16, 21, 22, 26-32, and 50-100 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition comprising insulin or C-peptide of insulin and an enhancer compound which has a consistency that permits it to be processed into primary particles having a diameter less than 10 microns, said composition in the form of a dry powder, methods of administration of the pharmaceutical composition and devices containing the pharmaceutical composition, it does not reasonably provide enablement for generic pharmaceutical polypeptides set forth in the claims, methods of administration or devices containing the pharmaceutical composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The rejection is maintained for reasons made of record for claims 1-22 and 26-60 in Paper No. 24, mailed 4-28-98.

Applicants arguments have been carefully considered but are not persuasive for reasons set forth below. Applicants' argue that one skilled in the art would known how to treat other diseases in light of the art and teachings of the specification without undue experimentation. Applicants' first argue that the claims do not recite treatment of specific diseases. This is not persuasive, the claims are not merely compositions for respiratory delivery but pharmaceutical compositions. The term "pharmaceutical" indicates pharmaceutical use of the composition in treatment of disease. The specification clearly does not teach how to use the pharmaceutical composition in the treatment of any disease. The claims drawn to methods of administration specifically deliver pharmaceutically active peptides, and thus treatment of disease clearly falls within the scope of the instant claims. Applicants claims are not merely drawn to compositions per se but to pharmaceutical compositions which is given weight in an enablement rejection. Applicants claims are not merely drawn to methods of delivery of a peptide of interest, but a pharmaceutical peptide. Thus, the term "pharmaceutical" implicitly implies treatment of disease. The specification clearly lacks teaching of effective respiratory dosages of pharmaceutical peptides, other than insulin. Applicants also argue that one skilled in the art would realize that the peptides recited in the claims are useful in treatment of disease, this is not persuasive, the means for treatment and method of delivery of the pharmaceutical composition is respiratory. The treatment modalities of the use of the peptides in oral or intravenous methods does not speak to the predictability of delivery of respiratory pharmaceuticals. Clearly, at the time the invention was made respiratory delivery of pharmaceutical peptide drugs was considered highly unpredictable because the pharmacological kinetics of the peptide or protein are unpredictable, and the art also considered that both the amount and timing of peptide drug bioavailablity were unpredictable (Patton, J, WO 94/07514; see page 1-2). Thus, at the time of filing, the art was

not so developed that administration by the respiratory route of pharmaceutical reagent to achieve systemic delivery was predictable. The claims are drawn to respiratory *pharmaceutical* compositions and methods of systemic delivery of the *pharmaceutical* compositions by the respiratory route. Clearly, the specification must therefore teach how to treat disease and achieve systemic administration by the respiratory tract. Applicants provide pharmaceutical formulations of the Physicians Desk Reference (Exhibit C) which are used to treat disease. These pharmaceutical compositions are not respiratory compositions as claimed. These pharmaceutical compositions are not administered by the lower respiratory route by mouth. Therefore, even if one would known what diseases were associated with lowered levels of peptide hormones treat, the specification lacks dosages which achieve the appropriate systemic concentration by the respiratory route to achieve effective treatment as is required by a pharmaceutical composition. Applicants also provide evidence that some models (Exhibits D-G) were available to test for systemic therapeutic levels. This is not fully persuasive because the evidence is not commensurate in scope with the claims and the methods are drawn to respiratory delivery which is not taught by the references. Applicants allege that such tests are would be routine to one skilled in the art and thus would require only routine testing in view of the teaching of the specification. This is not persuasive because at the time the invention was made, respiratory delivery of systemic acting peptides was considered by the art to be unpredictable (Patton, J, WO 94/07514; see page 1-2). Thus, more than routine experimentation would be required by the skilled artisan. Applicants provide WO 96/19206 as evidence of the operability of the invention. This evidence is not commensurate in scope with the claims.

The rejection is maintained.

8. The rejection of claims 1, 3-12 under 35 U.S.C. 102(b) as being anticipated by Schipper et al (Pharmaceutic Research, 10(5):682-686, published May 1993) is maintained for reasons made of record in Paper No. 24, mailed 4-28-98.

Applicants allege that the process of Shipper would result in larger particles and particles of less than 10 microns in diameter maximizes deposition in the lungs. Applicants allege that Shipper does not describe or suggest a powder composition where at least 50% of the total mass of active compounds are particles of 10 microns or less. This is not persuasive the claims recite optional agglomerates. Moreover, the composition must be able to be processed into primary particles having a diameter less than 10 microns. The composition is "comprising" and is optionally agglomerates. The dry powder composition is "comprising" and is not limited to processed primary particles where 50% of the total mass of active compounds are primary particles of 10 microns or less. Applicants' declaration is not persuasive because it does not provide evidence to support the opinion that the agglomerates of the art are different from the claimed compositions.

New Rejections Based on Amendment

9. Claims 1-16 and 98-100 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Applicants have amended the claims to recite that the pharmaceutical composition is "non-hygroscopic". Applicants point to pages 12 and 14 for support for this characterization of the total pharmaceutical composition (peptide/enhancer). The passages of page 12 does not

support this characteristic of the pharmaceutical composition *per se* because it discusses the nature of the counterion for ionic enhancers may influence the powder properties such as hygroscopicity. It does not support the concept of a non-hygroscopic powder, it is merely a teaching that the choice of counterion in an ionic enhancer may influence powdering properties. It does not support the conception, that applicants had at the time of filing conceived of the invention as a non-hygroscopic powder. As to the passage of page 14, the passage discusses the properties of other additives to the polypeptide/enhancer combination and not characteristics of the dry powder formulation *per se*. It does not support the conception, that applicants had at the time of filing conceived of the invention as a non-hygroscopic powder.

Status of Claims

10. All claims stand rejected.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

12. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (703) 308-3995.

Patricia A. Duffy, Ph.D.
January 18, 1999

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1600